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For : PYRIDO- AND PYRIMIDOPYRIMIDINE DERIVATIVES AS
ANTI-PROLIFERATIVE AGENTS

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PRELIMINARY AMENDMENT "A"

Dear Sir:

Prior to examination and calculation of fees due, please amend the above-identified application as follows.

- ☒ Amendments to the Specification begin on page 2 of this paper.
- ☒ Amendments to the Claims are reflected in the listing of the claims which begins on page 3 of this paper.
- ☐ Amendments to the Drawings begin on page of this paper and include an attached replacement sheet.
- ☒ Remarks begin on page 13 of this paper.

AMENDMENTS TO SPECIFICATION

Please amend the title as follows:

PYRIDO- AND PYRIMIDOPYRIMIDINE DERIVATIVES AS ANTI-
PROFILERATIVE AGENTS

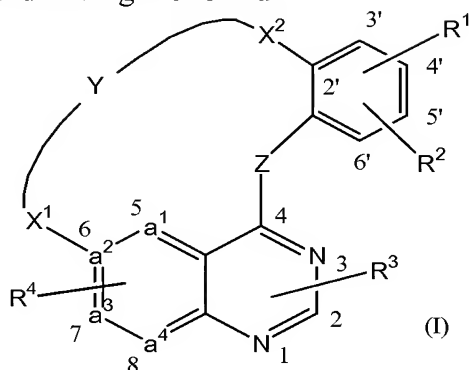
Page 1, between the Title and line 4, please insert the following new paragraph:

--Cross Reference to Related Applications

This application is the national stage of PCT Application No. Application No.
PCT/EP2004/053501, filed December 15, 2004, which application claims priority from
PCT Patent Application No. PCT/EP03/51062, filed December 18, 2003 and PCT
Patent Application No. PCT/EP03/51058, filed December 18, 2003, the entire
disclosures of which are hereby incorporated in their entirety.--

Listing of Claims

1. (Original) A compound having the formula



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

$a^1-a^2=a^3-a^4$ represents a divalent radical selected from $N-CH=CH-CH$, $N-CH=N-CH$ or $CH-CH=N-CH$;

Z represents O, NH or S;

Y represents $-C_{3-9}alkyl-$, $-C_{3-9}alkenyl-$, $-C_{1-5}alkyl-oxy-C_{1-5}alkyl-$,
 $-C_{1-5}alkyl-NR^{13}-C_{1-5}alkyl-$, $-C_{1-5}alkyl-NR^{14}-CO-C_{1-5}alkyl-$,
 $-C_{1-5}alkyl-CO-NR^{15}-C_{1-5}alkyl-$, $-C_{1-6}alkyl-CO-NH-$,
 $-C_{1-6}alkyl-NH-CO-$, $-CO-NH-C_{1-6}alkyl-$, $-NH-CO-C_{1-6}alkyl-$, $-CO-C_{1-7}alkyl-$,
 $-C_{1-7}alkyl-CO-$, $C_{1-6}alkyl-CO-C_{1-6}alkyl$;

X^1 represents a direct bond, O, $-O-C_{1-2}alkyl-$, CO, $-CO-C_{1-2}alkyl-$, NR^{11} ,
 $-NR^{11}-C_{1-2}alkyl-$, $NR^{16}-CO-$, $NR^{16}-CO-C_{1-2}alkyl-$, $-O-N=CH-$ or $C_{1-2}alkyl$;

X^2 represents a direct bond, O, $-O-C_{1-2}alkyl-$, CO, $-CO-C_{1-2}alkyl-$, NR^{12} ,
 $NR^{12}-C_{1-2}alkyl-$, $NR^{17}-CO-$, $NR^{17}-CO-C_{1-2}alkyl-$, $Het^{20}-C_{1-2}alkyl-$, $-O-N=CH-$ or
 $C_{1-2}alkyl$;

R^1 represents hydrogen, cyano, halo, hydroxy, formyl, $C_{1-6}alkoxy-$, $C_{1-6}alkyl-$,
 $C_{1-6}alkoxy-$ substituted with halo,
 $C_{1-4}alkyl$ substituted with one or where possible two or more substituents selected
from hydroxy or halo;

R^2 represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, Het^{16} -carbonyl-,
 $C_{1-4}alkyloxycarbonyl-$, $C_{1-4}alkylcarbonyl-$, aminocarbonyl-, mono-or
di($C_{1-4}alkyl$)aminocarbonyl-, Het^1 , formyl, $C_{1-4}alkyl-$, $C_{2-6}alkynyl-$, $C_{3-6}cycloalkyl-$,
 $C_{3-6}cycloalkyloxy-$, $C_{1-6}alkoxy-$, Ar^5 , Ar^1-oxy- , dihydroxyborane ,
 $C_{1-6}alkoxy-$ substituted with halo,

- C₁₋₄alkyl substituted with one or where possible two or more substituents selected from halo, hydroxy or NR⁵R⁶,
- C₁₋₄alkylcarbonyl- wherein said C₁₋₄alkyl is optionally substituted with one or where possible two or more substituents selected from hydroxy or C₁₋₄alkyl-oxy-;
- R³ represents hydrogen, C₁₋₄alkyl, cyano or C₁₋₄alkyl substituted with one or more substituents selected from halo, C₁₋₄alkyloxy-, amino-, mono- or di(C₁₋₄alkyl)amino-, C₁₋₄alkyl-sulfonyl- or phenyl;
- R⁴ represents hydrogen, hydroxy, Ar³-oxy, Ar⁴-C₁₋₄alkyloxy-, C₁₋₄alkyloxy-, C₂₋₄alkenyloxy- optionally substituted with Het¹² or R⁴ represents C₁₋₄alkyloxy substituted with one or where possible two or more substituents selected from C₁₋₄alkyloxy-, hydroxy, halo, Het²-, -NR⁷R⁸-, -carbonyl- NR⁹R¹⁰ or Het³-carbonyl-;
- R⁵ and R⁶ are each independently selected from hydrogen or C₁₋₄alkyl;
- R⁷ and R⁸ are each independently selected from hydrogen, C₁₋₄alkyl, Het⁸, aminosulfonyl-, mono- or di (C₁₋₄alkyl)-aminosulfonyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyl-oxy-C₁₋₄alkyl-, hydroxycarbonyl-C₁₋₄alkyl-, C₃₋₆cycloalkyl, Het⁹-carbonyl-C₁₋₄alkyl-, Het¹⁰-carbonyl-, polyhydroxy-C₁₋₄alkyl-, Het¹¹-C₁₋₄alkyl- or Ar²-C₁₋₄alkyl-;
- R⁹ and R¹⁰ are each independently selected from hydrogen, C₁₋₄alkyl, C₃₋₆cycloalkyl, Het⁴, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl- or polyhydroxy-C₁₋₄alkyl-;
- R¹¹ represents hydrogen, C₁₋₄alkyl, Het⁵, Het⁶-C₁₋₄alkyl-, C₂₋₄alkenylcarbonyl- optionally substituted with Het⁷-C₁₋₄alkylaminocarbonyl-, C₂₋₄alkenylsulfonyl-, C₁₋₄alkyloxyC₁₋₄alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C₁₋₄alkyloxy-;
- R¹² represents hydrogen, C₁₋₄alkyl, C₁₋₄alkyl-oxy-carbonyl-, Het¹⁷, Het¹⁸-C₁₋₄alkyl-, C₂₋₄alkenylcarbonyl- optionally substituted with Het¹⁹-C₁₋₄alkylaminocarbonyl-, C₂₋₄alkenylsulfonyl-, C₁₋₄alkyloxyC₁₋₄alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C₁₋₄alkyloxy-;
- R¹³ represents hydrogen, C₁₋₄alkyl, Het¹³, Het¹⁴-C₁₋₄alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C₁₋₄alkyloxy-;
- R¹⁴ and R¹⁵ are each independently selected from hydrogen, C₁₋₄alkyl, Het¹⁵-C₁₋₄alkyl- or C₁₋₄alkyloxyC₁₋₄alkyl-;
- R¹⁶ and R¹⁷ are each independently selected from hydrogen, C₁₋₄alkyl, Het²¹-C₁₋₄alkyl- or C₁₋₄alkyloxyC₁₋₄alkyl-;

- Het¹ represents a heterocycle selected from piperidinyl, morpholinyl, piperazinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het¹ is optionally substituted with one or where possible two or more substituents selected from amino, C₁₋₄alkyl, hydroxy-C₁₋₄alkyl-, phenyl, phenyl-C₁₋₄alkyl-, C₁₋₄alkyl-oxy-C₁₋₄alkyl- mono- or di(C₁₋₄alkyl)amino- or amino-carbonyl-;
- Het² represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het² is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C₁₋₄alkyl-, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyl-oxy-C₁₋₄alkyl-, hydroxy-C₁₋₄alkyl-oxy-C₁₋₄alkyl-, mono- or di(C₁₋₄alkyl)amino-, mono- or di(C₁₋₄alkyl)amino-C₁₋₄alkyl-, aminoC₁₋₄alkyl-, mono- or di(C₁₋₄alkyl)amino-sulfonyl-, aminosulfonyl-;
- Het³, Het⁴ and Het⁸ each independently represent a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het³, Het⁴ or Het⁸ is optionally substituted with one or where possible two or more substituents selected from hydroxy-, amino-, C₁₋₄alkyl-, C₃₋₆cycloalkyl-C₁₋₄alkyl-, aminosulfonyl-, mono- or di(C₁₋₄alkyl)aminosulfonyl or amino-C₁₋₄alkyl-;
- Het⁵ represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-;
- Het⁶ and Het⁷ each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het⁶ and Het⁷ are optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-;
- Het⁹ and Het¹⁰ each independently represent a heterocycle selected from furanyl, piperidinyl, morpholinyl, piperazinyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het⁹ or Het¹⁰ is optionally substituted C₁₋₄alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl- or amino-C₁₋₄alkyl-;

Het¹¹ represents a heterocycle selected from indolyl or  ;

- Het¹² represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het¹² is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C₁₋₄alkyl-, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyl-oxy-C₁₋₄alkyl-, hydroxy-C₁₋₄alkyl-oxy-C₁₋₄alkyl-, mono- or di(C₁₋₄alkyl)amino- or mono- or di(C₁₋₄alkyl)amino-C₁₋₄alkyl-;
- Het¹³ represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-;
- Het¹⁴ represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-;
- Het¹⁵ and Het²¹ each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het¹⁵ or Het²¹ are optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-;
- Het¹⁶ represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl, 1,3,2-dioxaborolane or piperidinyl wherein said heterocycle is optionally substituted with one or more substituents selected from C₁₋₄alkyl;
- Het¹⁷ represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-;
- Het¹⁸ and Het¹⁹ each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het¹⁸ and Het¹⁹ are optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-;
- Het²⁰ represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl, piperidinyl, piperazinyl or pyrazolidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy-C₁₋₄alkyl-, C₁₋₄alkyloxyC₁₋₄alkyl or polyhydroxy-C₁₋₄alkyl-; and

Ar¹, Ar², Ar³, Ar⁴ and Ar⁵ each independently represent phenyl optionally substituted with cyano, C₁₋₄alkylsulfonyl-, C₁₋₄alkylsulfonylamino-, aminosulfonylamino-, hydroxy-C₁₋₄alkyl-, aminosulfonyl-, hydroxy-, C₁₋₄alkyloxy- or C₁₋₄alkyl.

2. (Original) A compound according to claim 1 wherein;

Z represents NH;

Y represents -C₃₋₉alkyl-, -C₂₋₉alkenyl-, -C₁₋₅alkyl-oxy-C₁₋₅alkyl-, -C₁₋₅alkyl-NR¹³-C₁₋₅alkyl-, -C₁₋₅alkyl-NR¹⁴-CO-C₁₋₅alkyl-, -C₁₋₆alkyl-NH-CO-, -CO-C₁₋₇alkyl-, -C₁₋₇alkyl-CO- or C₁₋₆alkyl-CO-C₁₋₆alkyl;

X¹ represents O, -O-C₁₋₂alkyl-, -O-N=CH-, NR¹¹ or -NR¹¹-C₁₋₂alkyl-; in a particular embodiment X¹ represents a direct bond, C₁₋₂alkyl-, -O-C₁₋₂alkyl-, -NR¹¹-, -O- or -O-CH₂-;

X² represents a direct bond, O, -O-C₁₋₂alkyl-, -O-N=CH-, NR¹⁷-CO-, NR¹⁷-CO-C₁₋₂alkyl-, C₁₋₂alkyl, Het²⁰-C₁₋₂alkyl-, NR¹² or NR¹²-C₁₋₂alkyl-; in a particular embodiment X² represents a direct bond, C₁₋₂alkyl-, -O-C₁₋₂alkyl, NR¹⁷-CO-, NR¹⁷-CO-C₁₋₂alkyl-, Het²⁰-C₁₋₂alkyl-, -O- or -O-CH₂-;

R¹ represents hydrogen, cyano, halo or hydroxy, preferably halo;

R² represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, C₁₋₄alkyloxycarbonyl-, Het¹⁶-carbonyl-, C₁₋₄alkyl-, C₂₋₆alkynyl-, Ar⁵ or Het¹; in a further embodiment R² represents hydrogen, cyano, halo, hydroxy, or Ar⁵; in a more particular embodiment R² represents hydrogen or halo;

R³ represents hydrogen;

R⁴ represents hydrogen, hydroxy, C₁₋₄alkyloxy-, Ar⁴-C₁₋₄alkyloxy or R⁴ represents C₁₋₄alkyloxy substituted with one or where possible two or more substituents selected from C₁₋₄alkyloxy- or Het²-;

R¹¹ represents hydrogen, C₁₋₄alkyl- or C₁₋₄alkyl-oxy-carbonyl-;

R¹² represents hydrogen, C₁₋₄alkyl- or C₁₋₄alkyl-oxy-carbonyl-;

R¹³ represents hydrogen or Het¹⁴-C₁₋₄alkyl, in particular morpholinyl-C₁₋₄alkyl;

R¹⁴ represents hydrogen or C₁₋₄alkyl;

R¹⁷ represents hydrogen, C₁₋₄alkyl-, Het²¹-C₁₋₄alkyl or C₁₋₄alkyl-oxy-C₁₋₄alkyl; in particular R¹⁷ represents hydrogen or C₁₋₄alkyl;

Het¹ represents thiazolyl optionally substituted with amino, C₁₋₄alkyl, hydroxy-C₁₋₄alkyl-, phenyl, phenyl-C₁₋₄alkyl-, C₁₋₄alkyl-oxy-C₁₋₄alkyl-, mono- or di(C₁₋₄alkyl)amino- or amino-carbonyl-;

Het² represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het² is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C₁₋₄alkyl-;

In a further embodiment Het² represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C₁₋₄alkyl-, preferably methyl;

Het¹⁴ represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het¹⁴ is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C₁₋₄alkyl-;

Het¹⁶ represents a heterocycle selected from piperidinyl, morpholinyl or pyrrolidinyl;

Het²⁰ represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl or piperidinyl;

Het²¹ represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het²¹ is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C₁₋₄alkyl-;

Ar⁴ represents phenyl optionally substituted with cyano, hydroxy-, C₁₋₄alkyloxy or C₁₋₄alkyl-;

Ar⁵ represents phenyl optionally substituted with cyano, hydroxy, C₁₋₄alkyloxy or C₁₋₄alkyl.

3. (Original) A compound according to claim 1 wherein;

Z represents NH;

Y represents -C₃₋₉alkyl-, -C₁₋₅alkyl-NR¹³-C₁₋₅alkyl-, -C₁₋₅alkyl-NR¹⁴-CO-C₁₋₅alkyl-, -C₁₋₆alkyl-NH-CO- or -CO-NH -C₁₋₆alkyl- ;

X¹ represents -O-, -NR¹¹-, -NR¹⁶-CO-, or -NR¹⁶-CO-C₁₋₂alkyl-;

X² represents a direct bond, -C₁₋₂alkyl-, -O-C₁₋₂alkyl-, -O-, -O-CH₂- or Het²⁰-C₁₋₂alkyl-;

R¹ represents hydrogen or halo;

R² represents hydrogen, cyano, halo, hydroxycarbonyl-, C₁₋₄alkyloxycarbonyl-, Het¹⁶-carbonyl- or Ar⁵; in particular R² represents hydrogen or halo;

R³ represents hydrogen;

R⁴ represents hydrogen, hydroxy, C₁₋₄alkyloxy-, Ar⁴-C₁₋₄alkyloxy or R⁴ represents C₁₋₄alkyloxy substituted with one or where possible two or more substituents selected from C₁₋₄alkyloxy- or Het²-;

R¹¹ represents hydrogen;

R¹² represents hydrogen, C₁₋₄alkyl- or C₁₋₄alkyl-oxy-carbonyl-;

R¹³ represents hydrogen or Het¹⁴-C₁₋₄alkyl, in particular hydrogen or morpholinyl-C₁₋₄alkyl;

Het² represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het² is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C₁₋₄alkyl-;

In a further embodiment Het² represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C₁₋₄alkyl-, preferably methyl;

Het¹⁴ represents morpholinyl;

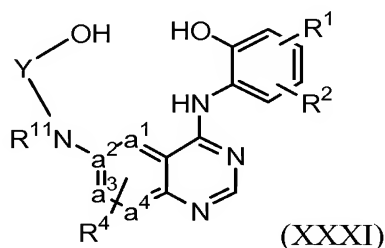
Het¹⁶ represents a heterocycle selected from morpholinyl or pyrrolidinyl;

Het²⁰ represents pyrrolidinyl or piperidinyl;

Ar⁴ represents phenyl;

Ar⁵ represents phenyl optionally substituted with cyano.

4. (Currently Amended) A compound according to claim 1 ~~or 2~~ wherein the R¹ substituent is at position 4', the R² substituent is at position 5', the R³ substituent is at position 3 and the R⁴ substituent at position 7 of the structure of formula (I).
5. (Currently Amended) A compound according to claim 1, ~~any one of claims 1 to 4~~ wherein a¹-a²=a³-a⁴ represents N-CH=CH-CH.
6. (Currently Amended) A compound according to claim 1, ~~any one of claims 1 to 4~~ wherein a¹-a²=a³-a⁴ represents N-CH=N-CH.
7. (Currently Amended) A compound according to claim 1, ~~any one of claims 1 to 4~~ wherein a¹-a²=a³-a⁴ represents CH-CH=N-CH.
8. (Currently Amended) A compound having the formula ~~An intermediate of formula~~



the N-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

a¹-a²=a³-a⁴ represents a divalent radical selected from N-CH=CH-CH or N-CH=N-CH;

Y represents -C₃₋₉alkyl-, -C₁₋₅alkyl-NR¹³-C₁₋₅alkyl-, -C₁₋₆alkyl-NH-CO- or -CO-NH-C₁₋₆alkyl-;

R¹ represents hydrogen or halo;

R² represents hydrogen, cyano, halo, hydroxycarbonyl-, C₁₋₄alkyloxycarbonyl-,
Het¹⁶-carbonyl- or Ar⁵;
R⁴ represents hydroxy, C₁₋₄alkyloxy-, Ar⁴-C₁₋₄alkyloxy or R⁴ represents C₁₋₄alkyloxy
substituted with one or where possible two or more substituents selected from
C₁₋₄alkyloxy- or Het²-;
R¹¹ represents hydrogen;
R¹³ represents Het¹⁴-C₁₋₄alkyl;
Het² represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or
pyrrolidinyl wherein said Het² is optionally substituted with one or where possible
two or more substituents selected from hydroxy, amino or C₁₋₄alkyl-;
Het¹⁴ represents morpholinyl;
Het¹⁶ represents a heterocycle selected from morpholinyl or pyrrolidinyl;
Ar⁴ represents phenyl;
Ar⁵ represents phenyl optionally substituted with cyano.

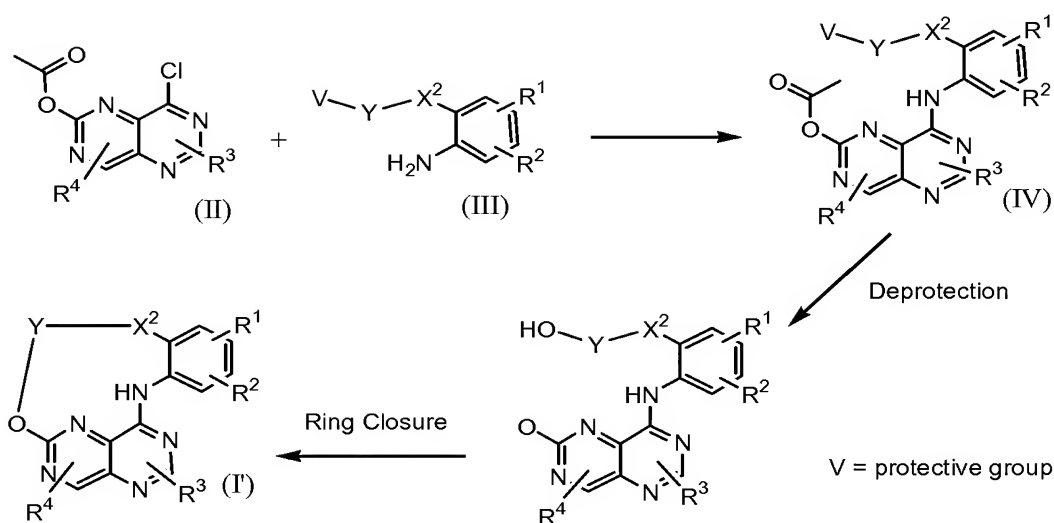
9-11. (Cancelled)

12. (Currently Amended) A pharmaceutical composition comprising a
pharmaceutically acceptable carrier and, as active ingredient, an effective kinase
inhibitory amount of a compound as claimed ~~described in claim 1~~ ~~any one of the~~
~~claims 1 to 7~~.

13.-14. (Cancelled)

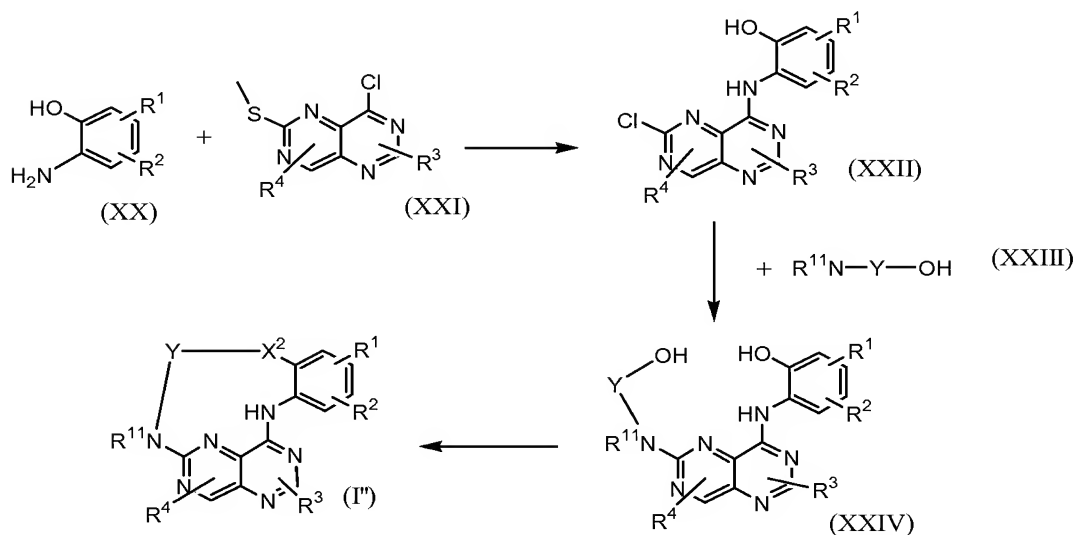
15. (Currently Amended) A pharmaceutical composition comprising a
pharmaceutically acceptable carrier and, as active ingredient, an effective kinase
inhibitory amount of a compound ~~an intermediate~~ as claimed in claim 6.

16. (Currently Amended) A process for preparing a compound as claimed in claims 1
to 7, comprising;
a) coupling 2-acetoxy-8-chloropyrimido[5,4-d]pyrimidine derivatives (II) with
suitable substituted anilines (III), to furnish the intermediates of formula (IV), and
deprotecting the intermediates of formula (IV) followed by ring closure under
suitable conditions;



; or

b) coupling the known 8-chloro-2(methylthio)-pyrimido[5,4-d]pyrimidine with 2-aminophenol derivatives of formula (XXI), yielding the intermediate compounds of formula (XXII), followed by animating the pyrido[3,2-d]pyrimidine of formula (XXII) ~~is aminated~~ using an aminated alcohol (XXIII) under art known conditions, followed by ring closure under Mitsunobu conditions to give the target compounds of formula (I'')



17. (Currently Amended) A method of treating a cell proliferative disorder, the method comprising administering to an animal in need of such treatment a therapeutically effective amount of a compound as claimed in claim 1 ~~any one of claims 1 to 7~~.

18. (Currently Amended) A method of treating a cell proliferative disorder, the method comprising administering to an animal in need of such treatment a therapeutically effective amount of a compound ~~an intermediate~~ as claimed in claim 8.

REMARKS

Consideration of the captioned application in view of the foregoing amendments and following remarks is requested.

The specification has been amended to refer to the priority applications.

Claims 1-8, 12 and 16-18 are currently pending. Claims 9-11 and 13-14 are hereby cancelled and claims 4-8, 12 and 16-18 are currently amended, without disclaimer of or prejudice to the subject matter deleted therein. No new matter has been added.

Accordingly, the claims pending and under consideration are claims 1-8, 12 and 16-18.

Early favourable action on the merits is respectfully requested.

Applicant respectfully requests that a timely Notice of Allowance of claims 11-8, 12 and 16-18 be issued in this case.

Respectfully submitted,

/Alana G. Kriegsman/

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